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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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LOUIS J. WILLE
BRISTOL-MYERS SQUIBB COMPANY
PATENT DEPARTMENT
P O BOX 4000
PRINCETON, NJ 08543-4000

EXAMINER	
TUCKER, ZACHARY C	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 12/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/616,365	CHENG ET AL.	
	Examiner	Art Unit	
	Zachary C. Tucker	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5,10,11,13-15 and 17-19* is/are pending in the application.

4a) Of the above claim(s) *17-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,10,11 and 13-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Note Change of Examiner

Applicants and applicants' counsel should note that Zachary C. Tucker, primary examiner in Group Art Unit 1624, is now charged with examination of this application.

Response to Amendment

As requested in the correspondence from applicants filed 23 January 2006 (hereinafter "present amendment"), which is in reply to the Office action mailed 11 October 2005 (hereinafter "previous Office action"), claims 1, 10, 11, 13 and 15 have been amended and claims 2, 4, 6-9, 12 and 16 have been cancelled. Also as requested, the abstract of the disclosure has been amended.

Status of Objection to Abstract

In the previous Office action, the abstract of the disclosure was objected to because it exceeded 25 lines of text in length. Objection to the abstract is hereby withdrawn in view of the present amendment thereto.

Election/Restrictions

Although it was not stated in the previous Office action, withdrawn claims 17-19, drawn to a pharmaceutical "combination," will be eligible for rejoinder under current PTO practice *re* Requirements for Restriction between products and methods of using the products and/or compositions comprised thereof, at such time that the claims of the elected Group, drawn to chemical compounds, methods of treatment comprising administering the compounds, and drawn to a pharmaceutical composition comprised of the compounds, are in condition for allowance [See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184

O.G. 86 (March 26, 1996)]. At such time of rejoinder, the Requirement for Restriction as was set forth in the previous Office action will be WITHDRAWN.

Some important observations pertaining to the withdrawn claims which are drawn to "pharmaceutical combinations" are provided hereinbelow in the section headed "Comments." Applicants are urged to consider these comments before responding to this Office action.

Currently, the conditions necessary to prompt rejoinder of the now-withdrawn claims have not as of yet been met; the Requirement is maintained. The claims of the elected restriction Group are not in condition for allowance.

Status of Claim Rejections - 35 USC § 112

In the previous Office action, claims 1-10 and 14-16 were rejected under the first paragraph of 35 U.S.C. 112, for lack of a disclosure that would enable one of ordinary skill in the chemical arts to prepare the full scope of all compounds embraced by the instant claims (whether said claims are drawn to chemical compounds *per se*, compositions comprised thereof or methods wherein said compounds are administered as a medical therapy).

In view of the present amendment to claim 1, which significantly narrows the scope of the claims describing the compounds, consequently narrowing in scope the compounds of which the composition and method are comprised, and also in view of applicants' argument accompanying said amendment (pages 17-20 of the correspondence filed 23 January 2006), the rejection is hereby withdrawn.

In the previous Office action, claims 15 and 16 were rejected further for lack of enablement, with respect to the claimed methods of treating various diseases and conditions in those claims. Cancellation of claim 16 renders moot the rejection of *that*

claim for alleged lack of enablement. Amendment of claim 15 to delete "and related diseases," referring to Type 2 diabetes, "inflammation," and "related diseases" referring to "atherosclerosis" has overcome in most part the finding of lack of enablement set forth in the previous Office action.

Instant claim 15, however, remains rejected under the first paragraph of 35 U.S.C. 112, for lack of enablement, because treatment of "diabetic complications" in general, is not found to be enabled by the accompanying disclosure.

The factual considerations from the decision rendered *In re Wands,* 858 F.2d 731,737 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) were outlined in the previous Office action at page 7. Each of the factors is reviewed in the following pages, with respect to the method for treating "diabetic complications" specified in claim 15.

(A) The term "diabetic complications" embraces a multitude of conditions and disease processes that result, either directly or indirectly from diabetes. The manner in which applicants have specified "diabetic complications" does not differentiate between complications arising from Type 1 diabetes and those arising from Type 2 diabetes – the term is recited simply "diabetic complications," as opposed to "complications of Type 2 diabetes," or "complications of Type 1 diabetes." As such, "diabetic complications" in general, would include, for example, neuropathy, nephropathy, retinopathy, elevated triglycerides, diabetic ketoacidosis, dry skin and fungal infection, but also more serious, secondary (and permanent, irreversible) complications of the diabetic disease process like gangrene, amputation, blindness, kindney failure, congestive heart failure, stroke, myocardial infarction, deep venous thrombosis, gastroparesis and erectile dysfunction.

(B) Instant claim 15 is drawn to a medical treatment method.

(C) State of the art with respect to treatment of "diabetic complications" is such that there is no single treatment modality which will remedy all complications of diabetes. Chronic hyperglycemia is the hallmark clinical sign of diabetes mellitus, and treatment of that condition is what constitutes a "treatment" for diabetes. Therapies for diabetes, whether Type 1 or 2, are aimed at maintaining normal blood glucose levels, in the fasting and post-absorptive state. The *complications* of the disease, once established (like, for example, stroke, or neuropathies, or kidney failure) cannot be treated by therapies aimed at maintaining normal blood glucose levels. Other interventions become necessary at that point. Some complications of diabetes cannot be treated at all. There is no treatment *per se* for blindness (which is the end result of prolonged and untreated diabetic retinopathy) or amputation (which is surgical intervention sometimes necessitated by the development of severe gangrene secondary to poor peripheral circulation, which is in turn due to diabetes). Complications like kidney failure (which is the result of prolonged untreated nephropathy) require totally different interventions than simply lowering blood sugar – kidney failure requires an organ transplant or hemodialysis. Erectile dysfunction is treated with vasodilator drugs, like sildenafil. Fungal infections must be treated with an appropriate antifungal agent.

(D) A physician specializing in the treatment of diabetes mellitus is the level of ordinary skill with respect to the method according to instant claim 15.

(E) Medicine is sometimes predictable, sometimes not. What can definitively be predicted in the case of the method according to instant claim 15 is that it is a medical impossibility that one therapeutic agent, namely, the compounds according to the present invention, will afford a plausible treatment for any and all complications of diabetes. According to applicants' disclosure of the invention, the compounds of the present

invention are effective for maintenance of euglycemia and lowering blood lipids, for example.

(F) There is no direction in the disclosure correlating to the full scope of instant claim 15. In fact, most of the above-mentioned (in point "A") complications of diabetes are not spoken to in the disclosure.

(G) There is no working example in the disclosure of the treatment of any complication of diabetes.

(H) It would not be possible with any amount of experimentation, for a physician of ordinary skill, to devise a method whereby all diabetic complications could be treated by administering a compound according to the present invention (according to instant claim 1) to a subject in need thereof. To do so is a practical impossibility.

In the previous Office action, claims 15 and 16 were rejected for indefiniteness under the second paragraph of 35 U.S.C. 112. The indefiniteness rejection of claims 15 and 16 is hereby withdrawn in view of the present amendment, which deletes "such as" from claim 15 and which cancels claim 16.

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New Claim Rejections - 35 USC § 112

Upon review of the claim set, the following new rejections are seen as necessary:

Claims 1,3,5,10,11 and 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, in the definition provide for variable "Y," the term "or a prodrug ester" appears. Given that a prodrug ester is a compound *per se*, and not a functional group on a

molecule, variable "Y" in the structure diagram specified in instant claim 1 cannot be a *prodrug ester*. In any case, specifying that "Y" is alternatively a "prodrug ester" is redundant, because the claim ends by specifying that the compounds of the invention may also be prodrug esters of those compounds described by the structural formula in the claim. It is a contradiction in terms for the substituent "Y" to be a "prodrug ester" and also for the compounds themselves, which are the subject of instant claim 1 to also be "prodrug esters" (alternatively).

Because all claims 3, 5, 10, 11, and 13-15 all depend from claim 1, all of those claims incorporate the limitations of an indefinite base claim and thus are rendered indefinite.

Obviousness-Type Double Patenting Rejections

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 5, 10, 11, 14 and 15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 11 and 12-14 of

U.S. Patent No. 7,105,556 (Cheng et al). Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 11 of the patent is drawn to three species, each of which is embraced by instant claims 1, 3, 5, 10 and 11, wherein "B" is a bond; R^1 is methyl; $-CH_2-CH_2-O-$; R^2 is H; "D" is a bond; "Y" is CO_2H; R^3 is alkoxyaryloxycarbonyl, arylalkylcarbonyl and aryloxyarylalkyl, respectively. Since claim 11 of the patent depends from claim 1 thereof, then claim 1 of the patent is not patentably distinct from instant claims 1, 3, 5, 10 and 11 either. Since claim 11 of the patent represents the most preferred species of the generic claim (claim 1) in that patent, and claims 12-14 of the patent each depend from that generic claim, then the pharmaceutical composition according to instant claim 14, and the method according to instant claim 15 are not patentably distinct from the pharmaceutical composition according to claim 12 of the patent and the methods according to claims 13 and 14 of the patent, respectively. The pharmaceutical composition and methods as specified in the claims of the patent are practiced with species from claim 11 thereof, and as such, the composition and method specified in the claims of the patent are not patentably distinct from the corresponding claims in the instant application.

Claims 1, 3, 5, 10, 11, 14 and 15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 13 and 15 of copending Application No. 11/406,799 (pursuant to the Preliminary Amendment filed in that application 19 April 2006). Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 1 of the copending application, although broadly generic, when interpreted in light of the accompanying disclosure, renders obvious the compounds of the present invention.

Specifically, if the disclosure of the copending application is consulted as a dictionary to provide a more specific understanding of what compounds applicants consider the invention in that application, at page 5 thereof, one finds that at least two of the preferred compounds of the invention are squarely within the scope of the instant claims. The fourth and fifth molecular structure representations on page 5 of the specification of the copending application are compounds according to instant claims 1, 3, 5, 10 and 11 wherein "B" is a bond; R^1 is methyl; $-CH_2-CH_2-O-$; R^2 is H; "D" is a bond; "Y" is CO_2H; R^3 is arylalkylcarbonyl and aryloxyarylalkyl, respectively. Thus, the pharmaceutical composition according to claim 13 of the copending application and the method for treating diabetes according to claim 15 of the copending application render obvious the corresponding composition and method of instant claims 14 and 15, respectively.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Comments, Claim Objections
~and~
Allowable Subject Matter

Claim 1 is objected to, in addition to being rejected as indefinite under 35 U.S.C. 112, second paragraph, and also for Obviousness-Type Double Patenting, because the term "alkyloxycarbonylaryloxycarbonyl" is repeated twice in the definition of variable "R^3."

Claim 15 is objected to, in addition to being rejected as indefinite under 35 U.S.C. 112, second paragraph, and also for Obviousness-Type Double Patenting, because the terms "dysmetabolic syndrome" and "Syndrome X" are synonyms. Applicant should choose one or the other; "Syndrome X" is the more common and readily recognized term.

In claim 15 also, the word "such" should be inserted in the penultimate line, between the word "of" and "treatment." This amendment, although quite simple, serves to

positively tie the treatment afforded by the method according to the claim, as recited in the preamble, to the method step of administering the compound according to claim 1 to a subject.

Deletion in claim 1 of the phrase "or a prodrug ester" in both occurrences in the definition of "Y" (or any place other than the latter part of the claim) will overcome the rejection of claims 1, 3,5, 10, 11 and 13-15 as indefinite under 35 U.S.C. 112, second paragraph.

No compound as represented by the structure diagrams of instant claim 13 is disclosed in or suggested by the prior art. Redrafting of claim 13 in independent form would overcome the indefiniteness rejection of that claim (on grounds that it depends from an indefinite base claim). No compound according to instant claims 1, 3, 5, 10 and 11, pharmaceutical composition according to claim 14 and method according to claim 15 is rendered obvious or anticipated by the prior art. The patent cited hereinabove in the section headed "Obviousness-Type Double Patenting Rejections" (US 7,105,556 (Cheng et al)) has a prior filing date under 35 U.S.C. 102(e), as of the filing date of the provisional application to which a claim for domestic priority is made, but is not available as prior art against the instant claims because the instant application and the patent were commonly owned at the time the present invention was made.

In addition to US 7,105,556, several related patents describe compounds similar in structure and function to those of the present invention. These are:

US 7,084,162,
US 7,053,106,
US 6,967,212,
US 6,919,358,
US 6,727,271,
US 6,653,314, and
US 6,414,002 (all to Cheng et al).

The '212 patent discloses compounds like those of the present invention, but the heterocyclic group at the position corresponding to the pyrrolidine ring in the compounds according to the present invention is instead the aromatic analog – pyrrole. Pyrrole does not render the fully saturated form thereof, pyrrolidine, obvious.

The remaining patents cited in the preceding list each disclose compounds like those of the present invention, but none of these patents disclose compounds comprising the pyrrolidine ring feature of the compounds of the present invention either. All of these other patents teach compounds that include an *acyclic* nitrogen atom at the part of the molecule where the pyrrolidine ring in the compounds of the present invention is found.

Should applicants file the appropriate disclaimers under 37 CFR 3.73(b), the double patenting rejections of claims 1, 3, 5, 10, 11, 14 and 15 would be overcome. If the indefiniteness rejection, the enablement rejection, and the double patenting rejection are all overcome, the claims of the elected Restriction Group will be in allowable form. Suggestions for the appropriate amendments are provided herein. The withdrawn claims in the application will be rejoined if, upon response to this Office action, the outstanding rejections are overcome. The Requirement for Restriction will be withdrawn at such time. There are some patentability issues with respect to the presently withdrawn claims, however.

Withdrawn claims 17-19 specify a "pharmaceutical combination." It is not clear whether these claims are intended to encompass a *method* wherein the respective agents are administered, or whether by the term "combination," applicants intended to describe a *composition* comprised of the respective agents. To avoid a rejection under the second paragraph of 35 U.S.C. 112, for indefiniteness, applicants are urged to replace the term "combination" with "composition" in instant claims 17-19.

Also in the withdrawn claims, it is noted that the term "a lipid modulating agent" literally reads on any agent which will either *lower* lipids or *raise* lipid levels. As such, foods high in saturated fats would qualify as applicants' "lipid modulating agent" specified in the "combination" according to instant claim 17 (withdrawn). The term "lipid-modulating agent" should be deleted, in favor of "lipid-lowering agent," recited immediately preceding.

In withdrawn claim 18, there are several classes of different therapeutic agents recited as additional components of the "pharmaceutical combination" specified in that claim. It is recommended that applicant exchange the commas separating each class of therapeutic agent for semicolons, to avoid ambiguity of one class being interpreted as including the other agents recited as part of another therapeutic class. Semicolons would more clearly delineate each class of agent from the others.

The term "a serotonin (and dopamine) reuptake inhibitor" is recited in claim 18, as one of the anti-obesity agents in the "pharmaceutical combination." It is not clear if this particular agent is required to be both a serotonin and dopamine reuptake inhibitor or if it is supposed to be a serotonin and/or dopamine reuptake inhibitor.

Lastly, in withdrawn claims 17 and 18, "and/or" is recited before the last *class* of additional therapeutic agent specified in the "pharmaceutical combination." If "and/or" in this case is operative as "and," then the claim reads on a "pharmaceutical combination" comprising a compound as defined in claim 1, and an additional therapeutic agent, which is all at the same time an antidiabetic agent, and anti-obesity agent, an antihypertensive agent, a platelet aggregation inhibitor, and an antiosteoporosis agent. There is no single agent which possesses all of these therapeutic utilities, or at least applicants have not identified any which are. The term "and/or" should in these occurrences (claims 17 and 18) be replaced with simply "or."

Should applicants amend the withdrawn claims in accordance with the suggestions found in the preceding paragraphs, the rejoinder of the withdrawn claims will not pose any new patentability issues.

Conclusion

Any inquiry concerning this communication should be directed to Zachary Tucker whose telephone number is (571) 272-0677. The examiner can normally be reached Monday to Friday from 5:45am to 2:15pm. If Attempts to reach the examiner are unsuccessful, contact the examiner's supervisor, James O. Wilson, at (571) 272-0661.

The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Zachary C. Tucker
Primary Examiner
Art Unit 1624